

WHAT IS CLAIMED IS:

1. A method of treating a botulinum toxin intoxication in a mammal comprising administering to a mammal an effective amount of at least one rescue agent.
2. The method of claim 1 wherein the rescue agent comprises an inactive botulinum toxin.
3. The method of claim 1 wherein the rescue agent comprises a compound selected from the group consisting of a modified nontoxic nonhemagglutinin, modified HA70 and HA34.
4. The method of claim 1 wherein the rescue agent comprises an inactive botulinum toxin and a modified nontoxic nonhemagglutinin.
5. The method of claim 2 wherein the inactive botulinum toxin comprises a light chain having the amino acid sequence set forth in SEQ ID NO:4.
6. The method of claim 2 wherein the inactive botulinum toxin has a reduced antigenicity.
7. The method of claim 6 wherein the inactive botulinum toxin has a mutated Hc region.
8. The method of claim 6 wherein the inactive botulinum toxin is glycosylated.
9. The method of claim 8 wherein the inactive botulinum toxin is glycosylated chemically.
10. The method of claim 8 wherein the inactive botulinum toxin is glycosylated by expression of the inactive botulinum toxin in a eukaryotic expression system.

11. The method of claim 10 wherein the eukaryotic expression system is a baculovirus expression system.
12. The method of claim 3 wherein the modified nontoxic nonhemagglutinin comprises a nontoxic nonhemagglutinin and a targeting moiety.
13. The method of claim 12 wherein the targeting moiety comprise a molecule which is recognized by and binds to a transporter of the liver and/or the kidney.
14. The method of claim 12 wherein the transporter is selected from the group consisting of P-gp, MRP2, BSEP, ABC transporters and mixtures thereof.
15. The method of claim 12 wherein the targeting moiety comprises at least one of a molecule selected from the group consisting of verapamil, cyclosporin A, tamoxifen, valsopodar, biricodar, tariquidar, zosuquidar, laniquidar, ONT-093, digoxin, digitalis or digitalis glycosides such as digitoxin, alpha-methyldigoxin, beta-acetyldigoxin and ouabain and mixtures thereof.
16. The method of claim 12 wherein the targeting moiety is chemically linked to the modified nontoxic nonhemagglutinin.
17. The method of claim 1 wherein the rescue agent comprises inactive botulinum toxin and a nontoxic nonhemagglutinin.
18. The method of claim 1 wherein the rescue agent is administered orally.
19. The method of claim 1 wherein the rescue agent is administered intravenously.
20. The method of claim 1 wherein the rescue agent is administered locally.

21. The method of claim 1 wherein the rescue agent is administered after the mammal has become intoxicated with a botulinum toxin.
22. A botulinum toxin which is glycosylated.
23. The botulinum toxin of claim 22 which is produced by a eukaryotic system.
24. The toxin of claim 23 wherein the eukaryotic system comprises an insect cell.
25. The toxin of claim 24 wherein the insect cell comprises a vector.
26. The toxin of claim 25 wherein the vector comprises a baculovirus.
27. The toxin of claim 22 wherein at least one of the Asn-xaa-Ser/Thr regions of the toxin is glycosylated.
28. The toxin of claim 22 wherein at least one of the Asn-Xaa-Cys regions of the toxin is glycosylated.
29. The toxin of claims 22 having reduced antigenicity.
30. The toxin of claims 22 or 29 wherein the toxin is inactive.
31. The toxin of claim 30 wherein the toxin is inactive botulinum toxin type A.
32. The toxin of claim 30 wherein a zinc binding motif of a light chain of the toxin is modified.
33. The toxin of claim 32 wherein the zinc binding motif comprises the sequence His-Glu-x-x-His (SEQ ID NO:1), wherein x is any amino acid.

34. The toxin of claim 32 wherein the modified zinc binding motif comprises Gly-Thr-x-x-Asn, (SEQ ID NO: 2).
35. The toxin of any of claims 22 or 29 wherein the toxin is botulinum toxin type A.
36. A method of treating a muscular condition, an autonomic nervous system disorder and/or pain comprising administering to the mammal in need any of the toxins in claims 22 to 29 or 31 to 35.
37. A botulinum toxin having reduced antigenicity.
38. The toxin of claim 37 which is produced by a eukaryotic system.
39. The toxin of claim 38 wherein the eukaryotic system comprises an insect cell.
40. The toxin of claim 39 wherein the insect cell comprises a vector.
41. The toxin of claim 40 wherein the vector comprises a baculovirus.
42. The toxin of claim 37 being glycosylated.
43. The toxin of claim 37 wherein at least one of the Asn-xaa-Ser/Thr regions of the toxin is glycosylated.
44. The toxin of claim 37 wherein at least one of the Asn-Xaa-Cys regions of the toxin is glycosylated.
45. The toxin of claim 37 wherein the toxin is modified to be inactive.

46. The toxin of claim 45 wherein the toxin is inactive botulinum toxin type A.
47. The toxin of claim 45 wherein a zinc binding motif of a light chain of the toxin is modified.
48. The toxin of claim 47 wherein the zinc binding motif comprises the sequence His-Glu-x-x-His (SEQ ID NO: 1), wherein x is any amino acid.
49. The toxin of claim 47 wherein the modified zinc binding motif comprises Gly-Thr-x-x-Asn, (SEQ ID NO: 2).
50. The toxin of any of claims 37 to 49 wherein the toxin is botulinum toxin type A.
51. A botulinum toxin having reduced antigenicity and is inactive.
52. A modified nontoxic nonhemagglutinin comprising a nontoxic nonhemagglutinin and a targeting moiety.
53. The nontoxic nonhemagglutinin of claim 52 wherein the targeting moiety comprise a molecule which is recognized by and binds to a transporter of a liver and/or a kidney.
54. The nontoxic nonhemagglutinin of claim 53 wherein the transporter is selected from the group consisting of P-gp, MRP2, BSEP, ABC transporters and mixtures thereof.
55. The nontoxic nonhemagglutinin of claim 52 wherein the targeting moiety comprises at least one of a molecule selected from the group consisting of verapamil, cyclosporin A, tamoxifen, valsopodar, biricodar, tariquidar, zosuquidar, laniquidar, ONT-093, digoxin, digitalis or digitalis glycosides such as digitoxin, alpha-methyldigoxin, beta-acetyldigoxin and ouabain and mixtures thereof.

56. The nontoxic nonhemagglutinin of claim 52 wherein the targeting moiety is chemically linked to the modified nontoxic nonhemagglutinin.

57. A method for making a di-chain botulinum in a non-Clostridium botulinum cell, the method comprises the step of expressing a single chain botulinum toxin and a nontoxic nonhemagglutinin in a non-Clostridium botulinum cell, whereby the nontoxic nonhemagglutinin facilitates the nicking of the single chain toxin into a di-chain toxin.

58. The method of claim 57 wherein the cell comprises a vector operatively harboring a nucleotide sequence encoding for the single chain toxin and a vector operatively harboring a nucleotide sequence encoding for the nontoxic nonhemagglutinin.

59. The method of claim 58 wherein the vector harboring a nucleotide sequence encoding for the single chain toxin also harbors a nucleotide sequence encoding for the nontoxic nonhemagglutinin.

60. The method of claim 57 wherein the vector is a baculovirus expression system.

61. The method of claim 57 wherein the cell is an eukaryotic cell.

62. The method of claim 61 wherein the cell is selected from the group consisting of PC12 cells, SHSY-5Y cells, HIT-T15 cells, HeLa cells, HEK293 cells, CHO cells, Neo 2 cells, yeast cells and plant cells.

63. The method of claim 57 wherein the di-chain botulinum toxin is an active botulinum toxin.

64. The method of claim 57 wherein the di-chain botulinum toxin is an inactive botulinum toxin.

65. A method of making a di-chain botulinum toxin in a cell free system, the method comprises the step of contacting a single chain botulinum toxin with a nontoxic nonhemagglutinin in a media, whereby the nontoxic nonhemagglutinin facilitates the nicking of the single chain toxin into a di-chain toxin

66. A non-Clostridial botulinum cell comprising a vector operatively harboring a nucleotide sequence encoding a single chain botulinum toxin and a vector operatively harboring nucleotide sequence encoding a nontoxic nonhemagglutinin.

67. The cell of claim 66 wherein the cell is selected from the group consisting of PC12 cells, SHSY-5Y cells, HIT-T15 cells, HeLa cells, HEK293 cells, CHO cells, Neo 2 cells, yeast cells and plant cells.

68. The cell of claim 66 wherein the vector harboring a nucleotide encoding a single chain botulinum toxin also harbors a nucleotide sequence encoding a nontoxic nonhemagglutinin.

69. The cell of claim 66 wherein the vector is a baculovirus expression system.

70. The toxin of claim 22 wherein the toxin is botulinum toxin type A.

71. The toxin of claim 29 wherein the toxin is botulinum toxin type A.

72. A method of treating a muscular condition, an autonomic nervous system disorder and/or pain comprising administering to the mammal in need any of the toxins in claim 30.